CERTIFICATE OF EXPRESS MAILING
"Express Mail" Mailing Label No.: ED 043241468 US
I hereby certify that this paper or fee is being deposited with the United States Postal Service with sufficient postage as first class "Express Mail Post Office to Addressee" service under 37 C.F.R. 1.10 on the date indicated below and is addressed to **MS: AMENDMENT**, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
Date of Deposit: August 31, 2004

Selena Whitaker-Paquiet

Attorney Docket No.: 13317.1001CIP
PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of **Peter KITE and David HATTON**

Group Art Unit: 1617

Application No.	:	10/659,413
Filed	:	September 10, 2003
For	:	**ANTISEPTIC COMPOSITIONS, SYSTEMS AND METHODS**
Examiner	:	Russell S. Travers

PETITION TO MAKE SPECIAL

MAIL STOP: AMENDMENT
Commissioner For Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir or Madam,

Applicants petition for accelerated examination pursuant to MPEP 708.02(VIII). The fee set forth in 37 CFR 1.17(h) accompanies this petition. Applicants are filing, herewith, a Preliminary Amendment canceling the claims, as filed, and introducing new claims 32-52. Applicants believe that all pending claims are directed to a single invention. If the Office determines that all claims are *not* obviously directed to a single invention, applicants will promptly make an election without traverse.

Claims 32-52 are pending as result of the Preliminary Amendment, filed herewith. A copy of pending claims 32-52 is attached hereto as Exhibit A.

This application is related as a continuation-in-part application to U.S. Patent Application No. 10/313,844 and the claimed subject matter is related. The '844 application was filed as PCT

International Patent Application PCT/US02/38863 and published on June 12, 2003, as WO 03/047341. A pre-examination search was made by the U.S. Patent and Trademark Office as the International Preliminary Search and Examination Authority in connection with PCT International Publication WO 03/047341. A copy of the International Search Report (ISR) is attached as Exhibit B. The ISR cited a single reference: U.S. Patent 4,258,056 of Lentsch. A Written Opinion mailed May 3, 2004 cited three additional prior art references: Root et al., "Inhibitory Effect of Disodium EDTA upon the Growth of Staphylococcus epidermidis In Vitro: Relation to Infection Prophylaxis of Hickman Catheters," *Antimicrobial Agents and Chemotherapy*, Nov. 1988, pp. 1627-1631; U.S. Patent 6,166,007 to Sodemann; and U.S. Patent 5,910,420 to Tuompo et al. A copy of the Written Opinion is attached as Exhibit C.

Claims 1-27 considered in the May 3, 2004 Written Opinion are directed to subject matter that is related to that of pending claims 32-52 in the subject patent application. The reasoned statement indicated that claims 1-27 were novel and had industrial applicability but lacked inventive step. The citations and detailed explanations are provided in the attached copy of the Written Opinion (Exhibit C). A copy of Applicants' Reply to the Written Opinion, filed July 2, 2004, presenting arguments in support of the claims having an inventive step, is attached as Exhibit D.

Applicants additionally have conducted searches and reviewed numerous references in connection with the evaluation and commercial development of the claimed antiseptic compositions, systems and methods. References believed by applicants and counsel to be potentially material to patentability were cited in an Information Disclosure Statement and accompanying form PTO-1449. Copies of these references were provided in connection with the Information Disclosure Statement. Copies of the Information Disclosure Statement(s) and PTO-Form 1449s citing references filed in connection with the subject U.S. patent application, including a Supplemental Information Disclosure Statement and PTO-Form 1449 filed herewith, are attached as Exhibit E. Copies of each of the references cited in each Information Disclosure Statement were provided at the time of filing the Statements and are therefore of record in this application.

Applicants provide, below, a brief statement of applicants' pending claims and a detailed discussion of the references deemed most relevant to applicants' pending claims. Exhibit F lists

the references cited in this Petition. Applicants do not concede that any of these references is "prior art" and reserve the right to antedate any of these references, by a showing under 37 C.F.R. §1.131 or otherwise. Applicants also provide statements explaining how the claimed subject matter is patentable over the references.

Applicants' claims are directed to an antiseptic composition comprising at least one salt of ethylene diamine tetraacetic acid (EDTA) and a solvent, wherein at least one EDTA salt comprises tetra-sodium EDTA and is at a concentration of at least 1.0% (w/v), wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes, and wherein the antiseptic composition has a pH of at least 9.5. Numerous dependent claims specify additional features of the antiseptic composition. Methods for inhibiting the growth and proliferation of microbial populations on various types of surfaces and objects, for substantially eradicating a broad spectrum of microbial populations, and for inhibiting the growth and proliferation of microorganisms in a biofilm matrix by contacting an object or surface with the claimed antiseptic compositions are also claimed.

Di-sodium EDTA has been used widely in various compositions, including as an anti-coagulant agent and to inhibit growth of certain bacterial populations. Data demonstrating the efficacy of tetrasodium EDTA compared to disodium EDTA has been generated by applicants and is presented in Figures 1A-1D of the present application. All of the microorganisms tested were clinical isolates and represent a broad spectrum of microbial populations. The data demonstrate that tetrasodium EDTA is a more effective bactericidal composition than disodium EDTA, particularly with regard to the non-*Staph* microorganisms. This is consistent with data presented and conclusions drawn by Root et al., in that Applicants' data demonstrates that *di-sodium* EDTA may be an effective inhibitory (and even bactericidal) agent against *Staph*. clinical isolates, but it does *not* have bactericidal activity against most of the other clinical isolates. Applicants' data demonstrates that reasonable concentrations of tetrasodium EDTA solutions, on the other hand, have inhibitory and bactericidal activity against all of the clinical isolates tested.

The pH of various EDTA salts in solution was recognized by applicants as an essential feature of applicants' antiseptic compositions. As noted in the specification of the subject patent application at the paragraph spanning pages 13 and 14, the British Pharmacopoeia (BP) specifies that a 5% solution of di-sodium EDTA has a pH of 4.0 to 5.5, and a solution of tri-sodium EDTA

has a pH of 7.0 to 8.0. Applicants' data, presented in Example 10, indicates that a 2% tetra-sodium EDTA solution has a pH of 11, while a 10% tetra-sodium EDTA solution has a pH of 11.6. Sodium EDTA salt preparations having a pH of 9.5 comprise a combination of tri-sodium and tetra-sodium EDTA salts.

Applicants' representative has reviewed all of the references cited to the USPTO in the Information Disclosure Statement(s) of record in this application and provides a detailed discussion of the following references, which are deemed by applicants' representative to be among the most relevant to patentability of the pending claims. A chart listing the references described herein is attached as Exhibit F.

Root et al. disclose that *disodium* EDTA and Vancomycin have an inhibitory effect on the growth of *Staphylococcus epidermidis* and suggest that EDTA should be *studied as a replacement for heparin solutions* for the "maintenance" of intravenous catheters *in granulocytopenic patients*, who are at risk of infection by *S. epidermidis*. The Root et al. model is specifically *based upon* ***disodium EDTA*** [See Col. 1, paragraph 3]. Neither the pH of the disodium EDTA solution nor the solvent is specified, but we must presume that the disodium EDTA solution was at an acidic or generally neutral pH. The authors note that microbiologists had previously studied the antibacterial action of disodium EDTA against various gram-negative organisms and that it has been used, in combination with other agents, for gram-positive infections. Applicants' review of the data presented in Root et al. demonstrates that what Root et al. show is that disodium EDTA has an inhibitory effect, not a *bactericidal* effect, against a single bacterial population, *S. epidermidis*. Applicants perceive no teaching or suggestion in the Root et al. reference to use an antiseptic composition comprising tetra-sodium EDTA and having a pH of at least 9.5.

Numerous references disclose the use of EDTA salt(s), in combination with one or more other agents, in combination compositions that have antimicrobial properties. Lentsch (U.S. Patent 4,258,056) discloses a composition for controlling mastitis comprising a "relatively concentrated, *buffered skin-pH* solution of a common anionic surfactant or detergent and a water soluble aminocarboxylic acid or aminocarboxylate chelating agent." [Col. 4, lines 25-28, emphasis added.] Compositions of this type "have been found to have excellent activity against the virulent gram positive mastitis-causing organisms under neutral or mildly acidic conditions,

e.g. *a pH of 4 to 7, more preferably below 6.5*." [Col. 4, lines 58-63, emphasis added.] EDTA salts are employed as the aminocarboxylic-type chelating agents. Lentsch notes at Col. 2, lines 53-54, that prior publications documented the lytic bactericidal action of "EDTA" on *Pseudomonas aeruginosa*, and that one of the publications noted that the bactericidal effect of EDTA was greater at pH 9.2 than at pH 7.8. [Col. 3, lines 1-3.] Lentsch also notes, at Col. 6, lines 2-48, that water soluble EDTA salts are used, with sodium or potassium salts being preferred, with the most preferred EDTA salt being disodium, *although other sodium EDTA salts are commercially available, including the tetra sodium salt.* Lentsch further notes, at the paragraph spanning Cols. 6 and 7, that *if* tetra-sodium or tetra-potassium EDTA is used, the buffer system counters the pH-raising effect of these salts. In this regard, Lentsch clearly teaches away from using tetrasodium EDTA and clearly teaches away from using any EDTA salt at a pH greater than physiological pH.

We reviewed the references referred to in the "Prior Art" section of Lentsch that were cited as support for the Examiner's statement in the PCT Written Opinion in the related PCT International patent application that "Lentsch further discloses that the bactericidal effect of EDTA is greater at a higher pH and that the use of tetrasodium salt increases the pH over that of the disodium salt." The article entitled "The Effect of Ethylenediamine-tetra-acetic Acid on the Cell Walls of Some Gram-Negative Bacteria," G.W. Gray and S.G. Wilkinson, *The Journal of General Microbiology*, Vol. 39, p. 385 (1965), found that EDTA has a "potent bactericidal action" against the cell walls of *two of the four* gram-negative bacterial populations tested based on experiments demonstrating that EDTA, at an *alkaline pH of 9.2* in borate buffer, selectively solubilized a high proportion of the carbohydrate and phosphorus present in the cell walls of sensitive organisms. Treatment with EDTA had little effect (as measured by a decrease in percentage turbidity) on the other two of the four bacterial populations tested. Such selective bactericidal activity does *not* suggest that this EDTA solution would have bactericidal efficacy against a broad spectrum of microorganisms or that it would be suitable as a lock-flush solution for conduits such as catheters. We also do not perceive any suggestion that use of an EDTA salt at a pH of at least 9.5 would be beneficial.

H. Haque and A.D. Russell, in "Effect of Ethylenediaminetetra-acetic Acid and Related Chelating Agents on Whole Cells of Gram-Negative Bacteria," *Antimicrobial Agents and*

Chemotherapy, Vol. 5, No. 5, pp. 447-452 (May 1974), observe that while EDTA is "particularly effective" against the pathogen *Pseudomonas aeruginosa*, it is not understood why other strains of gram-negative bacteria are considerably less susceptible to EDTA. The effects of EDTA buffered in pH 7.8 and 9.2 borate buffer solutions and other chelating agents were studied on seven strains of gram-negative bacteria and viability results are shown in Table 1. EDTA solutions at pH 9.2 generally produced a lower percentage viability than EDTA solutions at pH 7.8. The percentage viability for all bacterial strains, however, was *significant*, ranging from 9% to 88% viability after treatment with EDTA solution at pH 9.2. The authors conclude that CDTA (cyclohexane-1,2-diaminoetetraacetic acid) was the most active drug against all strains tested. These results do ***not*** support the use of CDTA or EDTA solutions, at either of the pH levels tested, as stand-alone antimicrobial agents. We also do not perceive any suggestion that use of an EDTA salt at a pH of at least 9.5 would be beneficial.

H. Haque and A.D. Russell, in "Effect of Chelating Agents on the Susceptibility of Some Strains of Gram-Negative Bacteria to Some Antibacterial Agents," *Antimicrobial Agents and Chemotherapy*, Aug. 1974, p. 200-206, study the effect of *pretreatment* with an EDTA solution (followed by treatment with a primary antibacterial agent), or *combination treatment* using EDTA or other chelating agents combined with a antibiotic or a non-antibiotic antibacterial agent on several strains of gram-negative bacteria. The EDTA solutions used to determine MIC were adjusted to pH 7.8 in a Tris buffer. The EDTA solutions used for pretreatment were in a Tris buffer at pH 9, mixed with a cell suspension in Tris buffer at pH 7.8. The results demonstrated that the MICs of non-antibiotic antibacterial agents were reduced in the presence of a chelating agent, with CDTA being the most effective chelating agent. The results also demonstrated that the chelating agents were more effective when used as a pretreatment agent prior to treatment with an antibacterial agent, rather than in combination with an antibacterial agent. We do not perceive any suggestion that a pretreatment or combination treatment using an EDTA salt in a composition having a pH of at least 9.5 would be beneficial or efficacious.

Sodemann (U.S. Patent 6,166,007) was cited in the Written Opinion for teaching disinfecting implanted devices such as catheters and ports, and for coating the exterior surfaces of catheters to prevent the deposition of blood coagula thereon and to thus prevent the growth of microbes (Col. 12, lines 44-58). Sodemann cites the Root et al. article as background research

and uses an antimicrobial lock composition comprising at least one taurinamide derivative *in combination with* an acid or salt to produce a *solution pH that is no higher than 7* [See Col 11, lines 30-60, emphasis added]. EDTA is listed as a potential acid and blood anticoagulant additive, and not as an antimicrobial. Although EDTA is listed as a potential anticoagulant, sodium citrate is preferred because of its pH lowering capability [See Col. 11, lines 30-60 and Col. 12, lines 24-43]. It is interesting to note that the antimicrobial compositions of Sodemann, like Lentsch, comprise EDTA in combination with a biocidal or antimicrobial agent, and both Sodemann and Lentsch prefer the combination to have an acidic pH in the range of less than 7. U.S. Patents 6,569,852 and 6,498,157 issued from divisional applications of the '007 patent and therefore contain the same disclosure. U.S. Patent 6,423,706 issued from a continuation-in-part application of the '007 patent and discloses taurolidine antimicrobial compounds in buffer solutions.

Tuompo et al. was cited in the Written Opinion for teaching use of an EDTA solution for the removal of biofilms. Applicants note that Tuompo et al. are pretreating object surfaces to remove biofilms prior to taking a sample for microbial analysis *and without hindering the growth of microorganisms*. Chemicals, such as a chelating agent (e.g. EDTA), detergent, alcohol, amine, reducing substance and/or hydrolytic enzyme/enzymes are used to detach the microbial mass from a surface so that microbes can be quantitatively analyzed *without hindering their growth*. EDTA (0.2-0.6%) was found to be the most efficient chelating agent tested for removing biofilms. This reference specifically discloses using a low concentration of EDTA, in combination with other agents, to *preserve* the viability of microorganisms while removing the biofilm matrix. Tuompo et al. clearly teach **against** the use and efficacy of EDTA as an antimicrobial agent and use EDTA at a concentration range outside the range recited in applicants' pending claims.

Several U.S. Patents and PCT publications directed to compositions comprising at least one anti-fungal agent and a chelator, methods, etc., show Issam Raad et al. as inventors. U.S. Patent 5,362,754 discloses pharmaceutical compositions of a mixture of minocycline and EDTA (M-EDTA) and methods of using the combination as a catheter flush solution to maintain the patency of a catheter port. M-EDTA solutions are also used to destroy and prevent the formation of polysaccharide-rich glycocalyx. The M-EDTA combination provides anticoagulant,

antimicrobial, glycocalyx inhibiting, antibacterial and antifungal activities for prevention of thrombogenesis, microbial adherence and device-related infections. Saline is an exemplary carrier solution. EDTA is used in a concentration of between about 10-100 mg/ml. The combination solution was adjusted to a physiologically acceptable *pH of about 7.4*. Example 3 shows EDTA (50 mg/ml) is effective to prevent adherent *S. epidermidis* colonies on a catheter surface. Example 7 also shows EDTA coating is effective to prevent biofilm deposition on catheter surfaces. We do not perceive any teaching or suggestion of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5 in this reference.

U.S. Patent 5,688,516 issued from an application that was a continuation-in-part of an application that was a continuation-in-part of the application that issued as U.S. Patent 5,362,754. The '516 patent discloses compositions including selected combinations of a chelating agent, anticoagulant, or antithrombotic agent, with a non-glycopeptide antimicrobial agent, such as the tetracycline antibiotics. Combinations of minocycline or other non-glycopeptide antimicrobial agents with EDTA, EGTA, DTPA, TTH, heparin and/or hirudin are disclosed for flushing and coating medical devices. The inventors note that EDTA may be excluded from the various compositions, with the compositions maintaining the desired therapeutic benefits. (*See*, Col. 4, lines 61-64.) Di-sodium EDTA was used in the experimental studies. The solutions were brought to a *physiologically acceptable pH of about 7.4*. (*See*, Col. 12, lines 62-63, emphasis added.) We do not perceive any teaching or suggestion of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5 in this reference.

WO 00/72906 A1 discloses kits for flushing medical devices and methods of preparing the flushing solution. The kit includes a dry mixture comprising a unit dose of a pharmacologically effective amount of an antimicrobial agent and a second agent selected from the group consisting of an anticoagulant, an antithrombotic agent, and a chelating agent. The antimicrobial agent may be selected from the group consisting of aminoglycoside, amphothericin B, ampicillin, carbenicillin, defazolin, cephalosporin, chloramphenicol, clindamycin, erythromycin, gentamicin, griseofulvin, kanamycin, methicillin, nafcillin, novobiocin, penicillin, polymyxin, rifampin, streptomycin, sulfamethoxazole, sulfonamide, tetracycline, trimethoprim, a phyarmacologically acceptable calcium salt, and a pharmacologically acceptable potassium salt. EDTA may be used as the anticoagulant with a carrier solution such as water, Ringers solution or

saline. A preferred kit comprises minocycline as the antimicrobial agent and EDTA. The concentration of EDTA in preferred embodiments is 30 mg/ml. The M-EDTA solutions were prepared as described in U.S. Patent 5,362,754, using disodium EDTA. Desirable pH ranges are not specified, but we presume the unit dose, when reconstituted with the carrier solution, provides a solution having a *generally physiological pH*, as taught in U.S. Patent 5,362,754. U.S. Patent 6,187,768 is a family member. We do not perceive any teaching or suggestion of an antiseptic composition for flushing medical devices comprising tetra-sodium EDTA having a pH of at least 9.5 in this reference.

WO 99/09997 discloses a method of treating a systemic fungal infection using a therapeutically effective amount of a pharmaceutical composition comprising at least one chelator; at least one antifungal agent; and a pharmaceutical excipient, diluent or adjuvant. Preferred chelators include EDTA, and the disodium trisodium, tetrasodium, dipotassium, tripotassium, dilithium and diammonium salts, as well as numerous chelates of EDTA and other compounds. Numerous antifungal agents are also disclosed as being useful. Monoclonal antibodies may be used to target particular fungal species. The inventors noted that the chelators they describe have significant growth inhibitory effect against species of *Aspergillus*; that EDTA exerts an inhibitory effect upon *Aspergillus flavus* relative to the control population; that similar inhibitory behavior was noticed in cultures of *Aspergillus terreus* and *Fusarium Oxysporum* following application of EDTA; and that the inhibitory effect of EDTA on *Candida krusei* was noticeable only a few hours after contact of the fungus with the chelator. The disodium salt of EDTA is a preferred chelator because of its demonstrated inhibitory effect upon target fungal pathogens. Desirable pH ranges are not specified for the described or experimental combination compositions. U.S. Patent 6,509,319 and 6,165,484 and published U.S. Application 2003/0032605 are family members and are related to one another as continuation applications. We do not perceive any suggestion of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5 in these references.

U.S. Patent 6,165,484 and U.S. Patent 6,509,319, which issued from a continuation application of the '484 patent, as well as U.S. Patent Application Publication US 2003/0032605 A1, which is a continuation of the '319 patent, are entitled "EDTA and Other Chelators with or without Antifungal Antimicrobial Agents for the Prevention and Treatment of Fungal

Infections." These disclosures teach that fungal infection may be a major cause of infection-related mortality in patients with leukemia and lymphoma, and that fungal infection is a major cause of mortality in patients with congenital and acquired deficiencies of the immune system. The inventors discovered that EDTA exerts an inhibitory effect upon *Aspergillus favus* relative to the control population. Similar inhibitory behavior was noted in cultures of *Aspergillus terreus* and *Fusarium oxysporum*, as well as *Candida krusei*. Various EDTA compositions, including the free acid, di-, tri- and tetra-sodium salts of EDTA and other EDTA salts, as well as many additional chelating agents are listed in Table 1 as useful chelating agents. The chelating and anti-fungal agents are delivered to desirable target sites systemically using monoclonal antibodies.

Experimental data are presented in Figs. 1-4 showing the inhibitory effect of EDTA on the various fungal species. No information relating to the EDTA solution(s) used, the concentration, pH, or other variables is given, nor are the experimental conditions described. Spectrophotometric absorbance increased less in colonies treated with EDTA, presumably indicating lower rates of replication. Additional data are presented in Figs. 5-11 to demonstrate a synergistic effect between EDTA and the anti-fungal agents Amphotericin B and Ambisome. Disodium EDTA was used. The combination of EDTA with the anti-fungal agent showed a synergistic effect compared to the action of either compound individually, and the population of viable cells was reduced in all cases. Only one of the fungal populations was eliminated (Figs. 9 and 11 – *Fusarium solani*), however, by treatment either with EDTA alone or the combination of EDTA with an anti-fungal agent. We do not perceive any teaching or suggestion of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5 in this reference.

EDTA and EDTA salts are disclosed as constituents of various cleaning solution combinations. U.S. Patent 2,474,412, for example, discloses soapless, germicidally active industrial cleaning compositions comprising the mono salt of EDTA with a germicidally active quaternary ammonium compound in water with water hardeners and strong electrolytes. The tetra alkali metal salt of EDTA is an effective precipitate inhibitor for use with germicidal quaternary ammonium salts and increases the germicidal activity. Mixtures may comprise from about 30% to 20% of the tetra-alkali metal salt of EDTA, with 20% being suitable for water of average hardness. 1 to 5 oz. of this mixture is diluted in 5 gallons of water. Where the pH of the

solution to which the germicidally active detergent mixture is to be added is under about 10, the pH of the mixture may be varied by the substitution of various amounts of the di- and tri-alkali metal salt for the tetra-alkali metal salt. (See, Col. 4, lines 52-58.) We do not perceive that this reference contains any teaching or suggestion of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5 that is suitable for use in connection with treatment of catheters, intravascular devices, or the other surfaces or devices specified in applicants' claims.

U.S. Patent 4,847,004 discloses a hard surface cleaning composition comprising a chelating agent including an alkali salt of EDTA and one or more surfactants. Tetrasodium EDTA is preferred and is disclosed as a well known component of detergent compositions. The EDTA component is present at a concentration of 4-40% by weight. pH ranges of the compositions are not given.

PCT International Patent Publication WO 02/072748 discloses a hard surface antimicrobial cleaner including a disinfectant and a polysiloxane. EDTA or its salts may be used optionally as a sequesterant, which may be used in an amount of 0.1% to 15% by weight. pH ranges for the compositions are not given. Tetra-sodium EDTA was used in experimental compositions in combination with several surfactants, disinfectant, solvent and alkali. The formulations demonstrated residual antimicrobial activity.

U.S. Patent 6,762,160 discloses compositions minimally comprising a detergent and a salt or salt-forming acid and, optionally, a bactericide. The detergent is preferably SDS; the salt or acid may be an EDTA salt or acid. *The preferred working pH is 5*. All of the tested acids were capable of dislodging biofilms, leaving the biofilm constituents free for the bactericidal activity of hydrogen peroxide. EDTA is considered as an activity enhancer. PCT International Publication WO 00/27438 discloses bactericidal and non-bactericidal solutions for removing biofilms that minimally comprise a detergent and a salt or salt-forming acid. The mixture may comprise, among other compounds, *1% EDTA at a pH higher than about 7.5*. We do not perceive any teaching or suggestion in these references of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

U.S. Patent 6,267,979 discloses combinations of a chelator with an antimicrobial agent to control biofouling in pipes and aqueous systems. EDTA and various EDTA salts may be used as the chelator, with the EDTA acid and disodium EDTA salt being most preferred of the EDTA

compounds. Numerous antifungal agents, biocides and antibiotics are disclosed as useful. Experimental data shows that EDTA (unspecified acid or salt) has an inhibitory effect on various microbial species. Disodium EDTA was used in synergy studies that demonstrated a synergistic effect of EDTA with gentamycin or polymyxin B against particular microbial species. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

EDTA has also been employed in blood diluent solutions. U.S. Patent 5,008,202 discloses that EDTA may be employed alone, or with sodium fluoride, as an antimicrobial reagent in a blood diluent comprising an organic buffer, a cell stabilizing agent, an inorganic salt, a solvent and EDTA. The solutions are adjusted to a *physiological pH of 6.9*. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

U.S. Patent 5,908,869 discloses propofol (2,6-diisopropylphenol) compositions for use as anesthetics in injectable oil-in-water emulsion solutions containing an anti-microbial agent. The emulsion is stabilized with a surfactant, and an edentate sufficient to prevent significant growth or microorganisms is added. Trisodium edentate, tetrasodium edentate and disodium calcium edentate are mentioned, and disodium edentate is most preferred to prevent significant growth of microorganisms for at least 24 hours in the event of adventitious extrinsic contamination. Microbial growth is reduced to no more than 10-fold increase following a low level of extrinsic contamination. The composition is formulated to be at *physiologically neutral pH*. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

U.S. Patent 6,350,251 discloses an access device providing a flow path between an external and internal patient site including a biocidal lock comprising an anticoagulant and a non-antibiotic biocide. EDTA and various EDTA salts are among the anticoagulants that may be used and are also among the non-antibiotic biocides that may be used. Taurinamide derivatives are preferred biocidal agents. *The pH range of the solution is 3.0-7*. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

U.S. Patent 6,429,225 discloses an antibacterial agent that inhibits growth of *Helicobacter pylori* for treatment of chronic gastritis and gastric ulcer comprising at least one substance consisting of EDTA acid and its metal salts. Sodium, calcium and iron EDTA salts are preferable. S olutions h aving a *pH of 8.0* were used experimentally. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

PCT International Patent Publication WO 02/05188 discloses locking implanted catheters with a solution comprising a lower alcohol, typically ethanol, propanol or butanol, most preferably i sopropanol, a nd a n a nti-microbial a dditive, t ypically t aurolidine o r t riclosan, o r a n anti-coagulant, which may be EDTA. The catheter body may be sufficiently porous to permit the anti-microbial solution of a lower alcohol to penetrate into the catheter body and preferably into the surrounding tissue. Desirable pH ranges for such solutions are not given. U.S. Patents 6,592,564 and 6,679,870 disclose lock solutions for implanted catheters comprising a lower alcohol, typically ethanol, propanol or butanol. The '870 patent discloses the combination of a lower alcohol with an additive comprising an anti-microbial, typically taurolidine or triclosan, or an anticoagulant, typically riboflavin, sodium citrate, EDTA or citric acid. We do not perceive any teaching or suggestion in these references of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

U.S. Patent 6,423,348 discloses an animal blood anticoagulant compound useful in the meat packing industry comprising tetrasodium EDTA (0.5-3.0%) in water with sodium hexametaphosphate, citric acid and sodium hydroxide to *balance the pH to 6.6-7.2*. We do not perceive a ny t eaching o r s uggestion i n t his r eference o f a n a ntiseptic c omposition c omprising tetra-sodium EDTA having a pH of at least 9.5.

U.S. Patent 5,300,296 discloses ophthalmic preparations comprising an industrial hydrophilic polymeric antimicrobial agent with additional agents including EDTA and alkali salts thereof and a boric acid borate buffer system. NPX, a broad spectrum polycationic antimicrobial agent, was combined with 0.08% by weight tetra-sodium EDTA and *buffered to pH 7* with a borate buffer system. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5 and at a concentration of at least 1.0% (w/v).

U.S. Patent 5,998,488 discloses the use of EDTA as part of an ophthalmic solution combination comprising an antimicrobial preservative having a quaternary ammonium type cationic group. Various EDTA salts may be used at a concentration of 0.006% to 0.1%. Boric acid or borax enhances the antimicrobial activity of the composition. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5 and at a concentration of at least 1.0% (w/v).

PCT International Publication WO 02/062260 discloses ophthalmic solutions containing select B vitamins, cationic preservatives, inositol, buffers, surfactants and/or other additives. A chelating agent (preferably disodium EDTA) may be added from 0.001 to 1 weight %, and/or an additional microbicide. The solution pH is *between 6.0 and 8.0* (*See*, page 5, emphasis added). We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

U.S. Patent 6,583,181 discloses that tetra-sodium salt of EDTA reduces ocular irritation and increases the disinfecting and sanitizing efficacy of quaternary ammonium compositions. Disinfectant solutions are useful for many applications, including institutional cleaning and sanitizing applications. EDTA acid is used in exemplary solutions, and there is no mention of suitable pH ranges. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

U.S. Patent 6,004,539 discloses an antimicrobial, abrasive (pumice) polishing compound, colloidal suspension or gel. The liquid phase may comprise up to about 0.1% each of preservative and chelating agent (e.g. salts of EDTA), and the liquid phase pH is adjusted to about 9.0 to 11.0. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5 *and* a concentration of at least 1.0% (w/v).

U.S. Patent 6,077,501 discloses a denture cleaning composition comprising a combination of a hexametaphosphate and an EDTA acid or salt. EDTA acid is preferred, but salts may also be used in concentration ranges of 1% - 15% by weight. *pH ranges of from about 6.5-8.5 are preferred*, with higher pH values tending to increase the cleaning effect of the combination. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

U.S. Patent 6,197,738 discloses a non-toxic sanitizing cleanser comprising an organic acid and chelating agent and surfactant. EDTA was used, e.g., at a concentration of 4% EDTA; the organic acid was used at a *pH <3*. The combination may be used in cosmetic lotion. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

PCT Publication WO 00/30460 discloses cleaning compositions for treating food such as produce comprising an anionic and/or nonionic detergent surfactant, electrolyte and basic buffer to provide a *pH of at least 8.5, and preferably higher*. Calcium disodium and disodium EDTA are among the dozens of compositions listed as suitable electrolytes. The amount of electrolyte employed is unspecified. Sodium and/or potassium EDTA is also listed as a suitable preservative at a level of from about 0.001% to about 3%, preferably from about 0.003% to about 0.2%, although the compositions don't generally require a preservative. Di-sodium EDTA is used at a nominal weight % of 0.003% in exemplary compositions E, F, G, H and R on pages 21 and 24 of the publication. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA at a concentration of at least 1.0% (w/v) and having a pH of at least 9.5.

Russell, A.D., in "*Ethylenediaminetetra-acetic Acid*," National Library of Medicine, Bethesda, Maryland, Academic Press Inc. (London) Ltd. pp. 209-224 (1971), cites extensive prior art literature showing that EDTA produces lysis in some bacteria but not in others. Only the sodium salts of EDTA possess antibacterial activity or can be used in the lysozyme-tris-EDTA system (p. 210). The role of buffers, particularly Tris, is important to the lytic activity on gram-negative bacteria. This reference cites literature stating that EDTA is only toxic to gram-negative bacteria other than *Pseudomonas* when used in conjunction with organic cations (p. 211). The author also notes that EDTA increases the sensitivity of various gram-negative bacteria to several substances and accelerates the death rate of starved bacteria. EDTA-Tris is used as a pretreatment increases sensitivity to some, but not all, bactericidal agents. EDTA was also used in combination with various antibacterial drugs. EDTA did not potentiate the activity of lysozyme against yeasts and moulds, but may have an effect on yeast protoplasts. A summary of the "antimicrobial activity" of EDTA is shown on p. 221, Table II. We do not perceive any

teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

Harper, W.E.S., et al., in "Effect of chlorhexidine/EDTA/Tris against bacterial isolates from clinical specimens," *Microbios*, 1987, pp. 107-112, Vol. 51, reports that a Chlorhexidine/EDTA/Tris combination was more active than chlorhexidine against several bacterial species. *Di-sodium EDTA* salt was used. Chlorhexidine solutions were tested at *pH of 7.4 or 8.4*, with no differences in results obtained. EDTA/Tris was effective against some isolates and much less effective against other isolates. The addition of EDTA/Tris to chlorhexidine markedly increased the antibacterial activity with effectiveness against most isolates. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

Kraniak, J.M., et al. in "Effect of Ethylenediaminetetraacetic Acid (EDTA) and Metal Ions on Growth of *Staphylococcus aureus* 196E in Culture Media," *Journal of Food Science*, 1988, pp. 910-913, Vol. 53, No. 3, disclose the effects of EDTA and its salts alone or in combination with cations on growth of an *S. aureus* strain. Data suggest that EDTA exerts its inhibitory effect by chelating calcium and/or other essential cations which form complexes with comparable stability constants with EDTA. All solutions were adjusted to *pH 7*. Growth of the S. *aureus* strain was inhibited by EDTA and its K and Na salts, but not by Fe or Ca salts. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

Bhagat et al., in "Growth response of *Pseudomonas stutzeri* RS34 to ethylenediaminetetraactic acid (EDTA) and its interaction with zinc," *Indian Journal of Experimental Biology*, July, 1993, pp. 590-594, Vol. 31, show the growth response of a *Pseudomonas stutzeri* strain that is less sensitive to the toxic effect of EDTA. *Disodium EDTA* was used, and the effect was more bacteristatic than bactericidal. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

Izzat and Bennett, in "Effect of varying concentrations of EDTA on the antimicrobial properties of cutting fluid preservatives," *Microbios* 26:37-44 (1979), studied EDTA and its disodium, trisodium and tetrasodium salts in combination with several cutting fluid

preservatives. The authors noted that a previous communication showed that EDTA has the capacity to potentiate the antimicrobial properties of a number of cutting fluid preservatives. In this paper, the authors observed that a ratio of 1 part preservative to 2 to 4 parts chelating agent (EDTA acid or salt) produced marked increases in antimicrobial action. It was noted that as the EDTA concentration was increased, the pH of samples dropped, and that the decreased activities noted with higher concentrations of EDTA may have resulted from pH factors. We do not perceive any teaching or suggestion in this reference of an antiseptic composition comprising tetra-sodium EDTA having a pH of at least 9.5.

It is urged that none of these prior art references, alone or in combination, discloses or suggests the subject matter of applicants' claims, namely, an antiseptic composition comprising at least one EDTA salt and a solvent, wherein at least one EDTA salt comprises tetra-sodium EDTA and is at a concentration of at least 1.0% (w/v), wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes, and wherein the antiseptic composition has a pH of at least 9.5.

Applicants request that their petition for accelerated examination be granted, and urge that the pending claims are allowable. Early allowance of the pending claims is respectfully requested.

– *Charge Deposit Account*

Please charge any fees that may be required, or credit any overpayment, to our Deposit Account No. 19-3555.

Respectfully submitted,

Ann W. Speckman
Registration No. 31,881

Date: August 31, 2004

SPECKMAN LAW GROUP PLLC

20601

Attorney Docket No.: 13317.1001CIP
PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of **Peter KITE and David HATTON**

Group Art Unit: 1617

Application No. : 10/659,413

Filed : September 10, 2003

For : **ANTISEPTIC COMPOSITIONS, SYSTEMS AND METHODS**

PENDING CLAIMS

Following Preliminary Amendment of August 31, 2004

32. An antiseptic composition comprising at least one salt of ethylene diamine tetraacetic acid (EDTA) and a solvent, wherein the at least one EDTA salt comprises tetra-sodium EDTA and is at a concentration of at least 1.0% (w/v), wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes, and wherein the antiseptic composition has a pH of at least 9.5.

33. An antiseptic composition of claim 32, wherein the at least one salt of EDTA comprises an EDTA salt selected from the group consisting of: di-sodium, tri-sodium and tetra-sodium EDTA salts and combinations thereof.

34. An antiseptic composition of claim 32, comprising tri-sodium and tetra-sodium EDTA.

35. An antiseptic composition of claim 34, wherein the antiseptic composition has a pH of at least 10.0.

36. An antiseptic composition of claim 32, comprising at least one EDTA salt at a concentration of at least 2.0%.

37. An antiseptic composition of claim 32, wherein the solvent comprises water and an alcohol.

38. An antiseptic composition of claim 37, comprising less than 10% (v/v) ethanol.

39. An antiseptic composition of claim 32, wherein the solvent comprises saline.

39. An antiseptic composition of claim 32 that is substantially free from an agent other than EDTA salt(s) having antimicrobial and/or anti-fungal activity that is at least 50% of the anti-microbial and/or antifungal activity of a sodium EDTA salt composition in aqueous solution at a concentration of 4% (w/v) and at a pH of 10.5.

40. An antiseptic composition of claim 32 formulated for topical application to surfaces and objects.

41. An antiseptic composition of claim 32 comprising tri- and tetra-sodium EDTA salts in an aqueous solvent at a concentration of between 2.0% and 8.0% (w/v) EDTA salt(s).

42. An antiseptic composition of claim 41, wherein the aqueous solvent is selected from the group consisting of: water, saline, and a mixture of water and an alcohol.

43. An antiseptic composition of claim 32 in a sterile, pyrogen-free form.

44. An antiseptic composition provided in a dry or partially hydrated formulation that, upon reconstitution with a solvent, forms an antiseptic composition of claim 1.

45. An antiseptic composition of either of claims 32 or 41 in sterile condition in a pre-filled syringe.

46. An antiseptic composition of either of claims 32 or 41 in a sterile condition in a single-dosage vial.

47. An antiseptic composition of either of claims 32 or 41 in a sterile condition in a multiple-dosage vial.

48. A method for inhibiting the growth and proliferation of microbial populations on a surface or object, comprising contacting the surface or object with an antiseptic composition of either of claims 32 or 41.

49. A method of claim 48, wherein the surface or object is selected from the group consisting of: catheters, medical tubes and conduits, intravascular devices and implanted medical devices.

50. A method of claim 48, wherein the surface or object is selected from the group consisting of: medical instruments and devices, contact lenses, optical implants, dental,

orthodontic and periodontal devices, water storage, distribution and treatment facilities, industrial equipment and food preparation and processing equipment.

51. A method for substantially eradicating a broad spectrum of microbial populations present on a device selected from the group consisting of catheters, medical tubes and conduits, intravascular devices and implanted medical devices, comprising contacting the device with an antiseptic composition of either of claims 32 or 41.

52. A method for inhibiting the growth and proliferation of microorganisms in a biofilm matrix comprising contacting an object or surface infected with microorganisms in a biofilm matrix with an antiseptic composition of either of claims 32 or 41.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/38863

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61L 2/18
US CL : 422/28; 510/434, 477; 514/566

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 422/28

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EDTA, tetra sodium, disinfectant

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4,258,056 A (LENTSCH) 24 March 1981 (24.03.81), see entire document, especially col.6, lines 39-42.	1-6

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
16 April 2003 (16.04.2003)

Date of mailing of the international search report
24 APR 2003

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. (703)305-3230

Authorized officer
Leigh McKane
Telephone No. 703-308-0661

Form PCT/ISA/210 (second sheet) (July 1998)

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
ANN W. SPECKMAN
SPECKMAN LAW GROUP
1501 WESTERN AVENUE, SUITE 100
SEATTLE, WA 98101

RECEIVED
MAY 06 2004
BY:

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of Mailing *(day/month/year)*	03 MAY 2004
Applicant's or agent's file reference P214246 (A)	REPLY DUE within 2 months/days from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US02/38863	05 December 2002 (05.12.2002)	05 December 2001 (05.12.2001)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61L 2/18 and US Cl.: 422/28; 510/434, 477; 514/566

Applicant

ASEPTICA, INC.

1. This written opinion is the first (first, etc,) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2 (a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension. See rule 66.2(d).~~

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*.
For an informal communication with the examiner, see Rule 66.6

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 05 April 2005 (05.04.2005).

Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer Leigh McKane Telephone No. 571-272-1700 Jean Proctor Paralegal Specialist

Form PCT/IPEA/408 (cover sheet)(July 1998)

WRITTEN OPINION

International application No.
PCT/US02/38863

I. Basis of the opinion

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:
pages 1-30, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages NONE, as originally filed
pages 19-20b, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the drawings:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."*

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	1-27	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	NONE	YES
	Claims	1-27	NO
Industrial Applicability (IA)	Claims	1-27	YES
	Claims	NONE	NO

2. CITATIONS AND EXPLANATIONS
Please See Continuation Sheet

Claims 1-27 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

TIME LIMIT:
The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

V. 2. Citations and Explanations:
Claims 1-6, 8, and 12-22 lack an inventive step under PCT Article 33(3) as being obvious over Root et al in view of Lentsch.

Root et al teaches a method for disinfecting a catheter by contacting the catheter (flushing) with an aqueous EDTA solution having a concentration of 20 mg/ml. The EDTA used by Root et al is in the form of the disodium salt. Lentsch, however, teaches that it is known in the art that both disodium and tetrasodium EDTA salts are available to one of ordinary skill in the art and that EDTA salts have a lytic bactericidal action (col.2, lines 53-54 and col.6, lines 30-31). Lentsch further discloses that the bactericidal effect of EDTA is greater at a higher pH and that the use of the tetrasodium salt increases the pH over that of the disodium salt. See col.3, lines 1-3 and col.6, lines 65-68. Therefore, it would have been obvious to one of ordinary skill in the art to substitute the tetrasodium salt of EDTA for the disodium salt employed by Root et al, as one would have expected to achieve a greater bactericidal effect.

Claims 7 and 9-11 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in the immediately preceding paragraph and further in view of Sodemann.

Root et al teaches the disinfecting of venous catheters but is silent to disinfecting an airway support device, a port, or a urological catheter. Sodemann discloses the use of antimicrobial agents for disinfecting other implanted devices such as various catheters and ports. See col.12, lines 44-67. As any type of device in contact with bodily fluids would be susceptible to microbial contamination, it would have been obvious to employ the method of Root et al with Lentsch to treat other body treatment devices.

Claims 23-25 lack an inventive step under PCT Article 33(3) as being obvious over Root et al in view of Lentsch and Tuompo et al.

Root et al teaches a method for disinfecting a catheter by contacting the catheter (flushing) with an aqueous EDTA solution having a concentration of 20 mg/ml. The EDTA used by Root et al is in the form of the disodium salt. Lentsch, however, teaches that it is known in the art that both disodium and tetrasodium EDTA salts are available to one of ordinary skill in the art and that EDTA salts have a lytic bactericidal action (col.2, lines 53-54 and col.6, lines 30-31). Lentsch further discloses that the bactericidal effect of EDTA is greater at a higher pH and that the use of the tetrasodium salt increases the pH over that of the disodium salt. See col.3, lines 1-3 and col.6, lines 65-68. Therefore, it would have been obvious to one of ordinary skill in the art to substitute the tetrasodium salt of EDTA for the disodium salt employed by Root et al, as one would have expected to achieve a greater bactericidal effect. Root et al does not disclose if the EDTA is effective against biofilms. However, Tuompo et al teaches that it was known in the art to employ an EDTA solution for the removal of biofilms. See col.12, lines 23-27. As Tuompo et al evidences that EDTA is effective in destroying the structure of biofilms, it would have been obvious to use the method of Root et al to treat biofilms existing on catheters.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Claims 26 and 27 lack an inventive step under PCT Article 33(3) as being obvious over Root et al in view of Lentsch and Sodemann.

Root et al teaches a method for disinfecting a catheter by contacting the catheter (flushing) with an aqueous EDTA solution having a concentration of 20 mg/ml. The EDTA used by Root et al is in the form of the disodium salt. Lentsch, however, teaches that it is known in the art that both disodium and tetrasodium EDTA salts are available to one of ordinary skill in the art and that EDTA salts have a lytic bactericidal action (col.2, lines 53-54 and col.6, lines 30-31). Lentsch further discloses that the bactericidal effect of EDTA is greater at a higher pH and that the use of the tetrasodium salt increases the pH over that of the disodium salt. See col.3, lines 1-3 and col.6, lines 65-68. Therefore, it would have been obvious to one of ordinary skill in the art to substitute the tetrasodium salt of EDTA for the disodium salt employed by Root et al, as one would have expected to achieve a greater bactericidal effect. Root et al does not disclose using the EDTA to coat the surface of the catheter. Sodemann discloses a method of catheter treatment wherein the catheter can be either flushed in the manner of Root et al or it can be coated. See col.1, lines 11-13. As Sodemann teaches that coating the exterior surfaces of catheters prevents the deposition of blood coagula thereon and thus, will prevent the growth of microbes (col.12, lines 44-58) thereon it would have been an obvious modification to the method of Root et al.

---------- NEW CITATIONS ----------

ROOT et al. "Inhibitory Effect of Disodium EDTA upon the Growth of Staphylococcus epidermis In Vitro: Relation to Infection Prophylaxis of Hickman Catheters." Antimicrobial Agents and Chemotherapy, Nov. 1988, pp.1627-1631.

US 6,166,007 A (SODEMANN) 26 December 2000 (26.12.2000), see col.12, lines 44-67.

US 5,910,420 A (TUOMPO et al) 08 June 1999 (08.06.1999), see col.12, lines 23-28.

CERTIFICATE OF EXPRESS MAILING
"Express Mail" Mailing Label No.: EU 984760317 US
I hereby certify that this paper or fee is being deposited with the United States Postal Service with sufficient postage as first class "Express Mail Post Office to Addressee" service under 37 C.F.R. 1.10 on the date indicated below and is addressed to MS: PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
Date of Deposit: July 2, 2004

Selena Whitaker-Paquiet

Attorney Docket No.: 13317.1001PCT
INTERNATIONAL PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: **ASEPTICA, INC.**

International Application No. : PCT/US02/38863

Filed : December 5, 2002

For : ANTI-MICROBIAL SYSTEMS AND METHODS

AMENDMENT AND REPLY TO WRITTEN OPINION

MAIL STOP: PCT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir or Madam:

Applicants request that claim pages 19-20a, attached as Exhibit A, be substituted for claim pages 19-20b previously being considered in this application. The substitute claim pages delete former claims 26 and 27 and otherwise do not make any amendments to the claims. Upon substitution of the attached claim pages, Claims 1-25 will be pending in this application.

Applicants also submit the following remarks in reply to the Written Opinion mailed May 3, 2004. This Reply is being filed within the two (2) months specified for reply. Consideration of Applicants' comments is respectfully requested prior to issuance of the International Preliminary Examination Report (IPER).

The Reasoned Statement provided with the May 3, 2004 Written Opinion indicated that pending claims 1-27 are novel and have industrial applicability. The claims were deemed not to involve an inventive step, however, in view of various combinations of prior art references. Claims 1-6, 8 and 12-22 were deemed to lack an inventive step as being obvious over Root et al. in view of Lentsch. Claims 7 and 9-11 were deemed to lack an

inventive step as being obvious over Root et al. in view of Lentsch and further in view of Sodemann. Claims 23-25 were deemed to lack an inventive step as being obvious over Root et al. in view of Lentsch and Tuompo et al. Claims 26 and 27 were deemed to lack an inventive step as being obvious over Root et al. in view of Lentsch and Sodemann. Applicants address each of these prior art references and various combinations of them below and urge that claims 1-27 do, indeed, involve an inventive step in view of the various combinations of the Root et al., Lentsch, Tuompo et al. and Sodemann references.

Applicants' claims are directed to a disinfectant composition and various uses of a disinfectant composition *consisting essentially of* an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have *a bactericidal* effect over a *broad spectrum of microbes* and a destructive effect against a variety of yeasts, and wherein *the EDTA salt comprises tetrasodium EDTA*. Claim 1, for example, recites a method for disinfecting a conduit by contacting the conduit with a disinfectant solution *consisting essentially of* an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have a bactericidal effect over a broad spectrum of microbes and a destructive effect against a variety of yeasts, and wherein *the EDTA salt comprises tetrasodium EDTA*. Claim 12 recites a method for disinfecting an object by contacting the object with the previously described disinfectant solution. Claim 15 specifically recites a method for disinfecting a catheter by contacting it with the disinfectant solution. Claim 23 recites a method for treating a biofilm by destroying the structure of the biofilm and killing or inhibiting the growth of individual organisms within the biofilm by contacting the biofilm with the disinfectant solution. Claim 19 is directed to the disinfectant solution *consisting essentially of* an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have a bactericidal effect over a *broad spectrum* of microbes and a destructive effect against a variety of yeasts, and wherein *the EDTA salt comprises tetrasodium EDTA.*

Root et al. disclose that *disodium* EDTA and Vancomycin have an inhibitory effect on the growth of *Staphylococcus epidermidis* and suggest that EDTA should be *studied as a replacement for heparin solutions* for the "maintenance" of intravenous catheters *in granulocytopenic patients*, who are at risk of infection by *S. epidermis*. The Root et al. model is specifically *based upon* ***disodium EDTA*** [See Col. 1, paragraph 3]. The authors note that microbiologists had previously studied the antibacterial action of ***disodium EDTA*** against various gram-negative organisms and that it has been used, *in combination with other agents*, for gram-positive infections. Applicants note that this is the *only* reference relied upon for rejection that discloses the use of a composition consisting essentially of an EDTA salt and a

solvent that has any antimicrobial activity whatsoever, and that this reference and the data it presents and conclusions it makes are specifically *based upon* ***disodium EDTA***. Furthermore, the data presented in Root et al. demonstrates that disodium EDTA has an inhibitory effect, not a *bactericidal* effect, against a single gram-positive strain of *S. epidermis*.

Table 1 in Root et al. shows the results of experiments in which solutions of disodium EDTA, heparin, Vancomycin and Vancomycin/heparin were applied on catheter surfaces 24 hours after inoculation with *S. epidermis* (10^3 CFU), and the adherence and growth of *S. epidermis* was measured after a 24 hour incubation period. The results show that the Vancomycin and Vancomycin/heparin solutions effectively killed the bacterial population, while significant bacterial populations remained on the catheter surfaces in contact with the disodium EDTA and Heparin solutions. The catheter surface in contact with the disodium EDTA solution had a substantially lower bacterial population than the catheter surface in contact with the Heparin solution, but the microbial population was significant and would pose a significant health threat. The experimental results shown in Table 2 demonstrate that, of the disodium EDTA concentrations tested using an inoculation of 10^3 CFU *S. epidermis*/ml, 20 mg/ml was the most effective and may have prevented attachment of bacteria to the catheter. Nonetheless, a significant bacterial population (0.7 $\log_{10}$ CFU/ml) was present in the culture medium 24 hours after inoculation. Table 3 demonstrates that, with inoculations of 10^5 CFU *S. epidermis*/ml, none of the disodium EDTA concentrations tested (up to 50 mg/ml) was effective to eliminate bacterial infections either on the catheter or in the medium. This data suggests that using a disodium EDTA solution reduces the population of an *S. epidermis* strain compared to using a heparin solution but does not eliminate the bacterial population, either on catheter surfaces or in the culture medium.

Root et al. demonstrated that disodium EDTA solutions have greater *S. epidermis* inhibitory activity than heparin solutions and far lower *S. epidermis* bactericidal activity than Vancomycin and concluded that disodium EDTA causes a *reduction* in viable organisms, even in the presence of catheter segments. Root et al. suggest the study of disodium EDTA as a replacement for heparin in catheter maintenance applications because the disodium EDTA has anticoagulant activity and has greater microbial inhibitory activity, at least against *S. epidermis*, than heparin. It is urged that one of ordinary skill in the art, reviewing Root et al., would conclude that disodium EDTA should be examined as a viable substitute for heparin in a catheter lock solution to provide anticoagulant and some inhibition of *S. epidermis* microbial infections. One of ordinary skill in the art would also note that disodium

EDTA alone does not, at any concentration or any inoculation level of *S. epidermis*, serve as an effective *bactericidal* agent. One would thus conclude, based on the experimental work and discussion of Root et al., that a supplemental antimicrobial agent would be required, in combination with disodium EDTA, to provide a *bactericidal* effect over a *broad spectrum* of microbes and a destructive effect against a variety of yeasts.

Lentsch discloses a combination composition for controlling mastitis comprising a "relatively concentrated, buffered skin-pH solution of a common anionic surfactant or detergent and a water soluble aminocarboxylic acid or aminocarboxylate chelating agent." [Col. 4, lines 25-28.] Combinations of this type "have been found to have excellent activity against the virulent gram positive mastitis-causing organisms under neutral or mildly acidic conditions, e.g. a pH of 4 to 7, more preferably below 6.5." [Col. 4, lines 58-63.] EDTA salts are employed as the aminocarboxylic-type chelating agents. Lentsch notes at Col. 2, lines 53-54, that prior publications documented the lytic bactericidal action of "EDTA" on *Pseudomonas aeruginosa*, and that one of the publications noted that the bactericidal effect of EDTA was greater at pH 9.2 than at pH 7.8. [Col. 3, lines 1-3.] Lentsch also notes, at Col. 6, lines 2-48, that water soluble EDTA salts are used, with sodium or potassium salts being preferred, with the most preferred EDTA salt being **disodium**, although Lentsch notes that other sodium EDTA salts are commercially available, including the *tetra sodium salt.*

Lentsch discloses, at most, that tetrasodium EDTA was commercially available and may be used as a substitute, albeit a non-preferred substitute, for disodium EDTA in mastitis compositions additionally comprising an anionic surfactant or detergent that provides antimicrobial activity. Lentsch teaches that omitting the anionic surfactant from the combination composition reduces the activity against gram positive microorganisms. [Col. 5, lines 41-43]. This teaching clearly indicates that the EDTA component of the Lentsch combination composition is ***not*** an effective antimicrobial agent in the absence of an anionic surfactant or detergent.

We reviewed the references referred to in the "Prior Art" section of Lentsch that are cited as support for the Examiner's statement that "Lentsch further discloses that the bactericidal effect of EDTA is greater at a higher pH and that the use of tetrasodium salt increases the pH over that of the disodium salt." Copies of these references are provided for the Examiner's review at Exhibit B. The article entitled "The Effect of Ethylenediaminetetra-acetic Acid on the Cell Walls of Some Gram-Negative Bacteria," G.W. Gray and S.G. Wilkinson, *The Journal of General Microbiology*, Vol. 39, p. 385 (1965), found that EDTA has a "potent bactericidal action" against the cell walls of *two of the four* gram-negative

bacterial populations tested based on experiments demonstrating that EDTA, at an alkaline pH of 9.2, selectively solubilized a high proportion of the carbohydrate and phosphorus present in the cell walls of sensitive organisms. Treatment with EDTA had little effect (as measured by a decrease in percentage turbidity) on the other two of the four bacterial populations tested. Such selective bactericidal activity does *not* suggest that this EDTA solution would have bactericidal efficacy against a broad spectrum of microorganisms or that it would be suitable as a lock-flush solution for conduits such as catheters.

H. Haque and A.D. Russell, in "Effect of Ethylenediaminetetraacetic Acid and Related Chelating Agents on Whole Cells of Gram-Negative Bacteria," *Antimicrobial Agents and Chemotherapy*, Vol. 5, No. 5, pp. 447-452 (May 1974), observe that while EDTA is "particularly effective" against the pathogen *Pseudomonas aeruginosa*, it is not understood why other strains of gram-negative bacteria are considerably less susceptible to EDTA. The effects of EDTA buffered in pH 7.8 and 9.2 solutions and other chelating agents were studied on seven strains of gram-negative bacteria and viability results are shown in Table 1. EDTA solutions at pH 9.2 generally produced a lower percentage viability than EDTA solutions at pH 7.8. The percentage viability for all bacterial strains, however, was *significant*, ranging from 9% to 88% viability after treatment with EDTA solution at pH 9.2. The authors conclude that CDTA (cyclohexane-1,2-diaminoetetraacetic acid) was the most active drug against all strains tested. These results do ***not*** support the use of CDTA or EDTA solutions, at either of the pH levels tested, as stand-alone antimicrobial agents.

H. Haque and A.D. Russell, in "Effect of Chelating Agents on the Susceptibility of Some Strains of Gram-Negative Bacteria to Some Antibacterial Agents," *Antimicrobial Agents and Chemotherapy*, Aug. 1974, p. 200-206, study the effect of *pretreatment* with an EDTA solution (followed by treatment with a primary antibacterial agent), or *combination treatment* using EDTA or other chelating agents combined with a antibiotic or a non-antibiotic antibacterial agent on several strains of gram-negative bacteria. EDTA is not used or proposed as a stand-alone antimicrobial agent. The results demonstrated that the MICs of non-antibiotic antibacterial agents were reduced in the presence of a chelating agent, with CDTA being the most effective chelating agent. The results also demonstrated that the chelating agents were more effective when used as a pretreatment agent prior to treatment with an antibacterial agent, rather than in combination with an antibacterial agent.

Root et al. worked specifically and exclusively with *disodium* EDTA and did not disclose or suggest that other EDTA salts may have similar properties or may be useful substitutes for heparin solutions used to treat indwelling catheters, although we may conclude

that tetrasodium EDTA was commercially available to Root et al. Root et al. also did not propose the use of disodium EDTA as a stand-alone, broad spectrum disinfectant, but rather as an anticoagulant having some inhibitory microbial activity against a single strain of *S. epidermis*. It is urged that it would ***not*** have been obvious to one of ordinary skill in the art to substitute the tetrasodium EDTA that was disclosed as commercially available and non-preferred by Lentsch, and only in combination with an anionic surfactant, for the disodium EDTA salt used by Root et al., particularly in light of the teaching, in Lentsch, that an anionic surfactant or detergent is *required* for satisfactory antimicrobial activity. It is urged that combination of the teachings of Root et al. and Lentsch does **not** suggest Applicant's claimed compositions and methods, which require a disinfectant composition *consisting essentially of* an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have a *bactericidal effect over a broad spectrum of microbes* and a destructive effect against a variety of yeasts, and wherein *the EDTA salt comprises tetrasodium EDTA*.

The Examiner relies on Sodemann for teaching disinfecting implanted devices such as catheters and ports, and for coating the exterior surfaces of catheters to prevent the deposition of blood coagula thereon and to thus prevent the growth of microbes (Col. 12, lines 44-58). Sodemann cites the Root et al. article as background research and uses an antimicrobial lock composition comprising at least one taurinamide derivative *in combination with* an acid or salt to produce a solution pH that is no higher than 7 [See Col 11, lines 30-60]. EDTA is listed as a potential acid and blood anticoagulant additive, and not as an antimicrobial. Although EDTA is listed as a potential anticoagulant, sodium citrate is preferred because of its pH lowering capability [See Col. 11, lines 30-60 and Col. 12, lines 24-43].

It is interesting to note that the antimicrobial compositions of Sodemann, like Lentsch, comprise EDTA *in combination with* a biocidal or antimicrobial agent, and both Sodemann and Lentsch prefer the combination to have an acidic pH in the range of less than 7. Sodemann does **not** remedy the deficiencies of Lentsch and Root et al. with respect to the patentability of and inventive step demonstrated by Applicants' pending claims. Applicants urge that no combination of the teachings of Root et al., Lentsch and Sodemann would suggest a disinfectant composition *consisting essentially of* an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have a *bactericidal* effect over a *broad spectrum of microbes* and a destructive effect against a variety of yeasts, and wherein *the EDTA salt comprises tetrasodium EDTA*.

Tuompo et al. is cited for teaching use of an EDTA solution for the removal of biofilms. Applicants note that Tuompo et al. are pretreating object surfaces to remove

biofilms prior to taking a sample for microbial analysis *and without hindering the growth of microorganisms.* Chemicals, such as a chelating agent (e.g. EDTA), detergent, alcohol, amine, reducing substance and/or hydrolytic enzyme/enzymes are used to detach the microbial mass from a surface so that microbes can be quantitatively analyzed *without hindering their growth.* EDTA (0.2-0.6%) was found to be the most efficient chelating agent tested for removing biofilms. This reference specifically discloses using EDTA, in combination with other agents, to *preserve* the viability of microorganisms while removing the biofilm matrix. Tuompo et al. clearly teach **against** the use and efficacy of EDTA as an antimicrobial agent, while Applicant's claims specify that the EDTA salt comprising tetrasodium EDTA is at a concentration sufficient to have *a bactericidal effect over a broad spectrum of microbes* and a destructive effect against a variety of yeasts.

The subject patent application presents data in support of the claims to disinfectant compositions and uses of the disinfectant compositions. Exhibits A1 and A2 of the subject application show the MIC (Minimum Inhibitory Concentration) and MBC (Minimum Bactericidal Concentration) of tetrasodium EDTA solutions (among others) required to inhibit growth (MIC) and kill the entire population (MBC) of numerous microorganisms. MIC and MBC experimental data is presented for twelve (12) *Staphylococcus* isolates; five (5) Methicillin-resistant *S. aureus* isolates; two (2) Vancomycin-resistant *Enterococci* isolates; two (2) *Enterococcus* isolates; four (4) *Klebsiella* isolates; three (3) *Escherichia* isolates; three (3) *Enterobacter* isolates; one (1) *Stenotrophomonas* isolate; three (3) *Pseudomonas* isolates; two (2) *Coryneform* isolates; two (2) *Acinetobacter* isolates; and three (3) *Proteus* isolates. Exhibit C shows MIC and MBC experimental data for nine (9) yeast populations. The organisms used in the testing are all clinical isolates and represent a broad spectrum of microbial populations, many of which produce serious, even lethal infection if they are introduced to a patient's blood stream. This data demonstrates that reasonable concentration of tetrasodium EDTA solutions have *a bactericidal effect over a broad spectrum of microbes,* and a destructive effect on a variety of yeasts.

Data demonstrating the efficacy of tetrasodium EDTA compared to disodium EDTA has been generated by applicants and is presented at Exhibit C. This data and the experimental conditions used to generate the data are described in U.S. Patent Application Publication No. US 2004/0110841 A1, published June 10, 2004. All of the microorganisms tested are clinical isolates and represent a broad spectrum of microbial populations. The data demonstrate that tetrasodium EDTA is a more effective bactericidal composition than disodium EDTA, particularly with regard to the non-*Staph* microorganisms. This is

consistent with data presented and conclusions drawn by Root et al., in that Applicants' data demonstrates that *di-sodium* EDTA may be an effective inhibitory (and even bactericidal) agent against *Staph.* clinical isolates, but it does *not* have bactericidal activity against most of the other clinical isolates. Applicants' data demonstrates that reasonable concentrations of tetrasodium EDTA solutions, on the other hand, have inhibitory and bactericidal activity against all of the clinical isolates tested.

Applicants' claimed disinfectant compositions consisting essentially of an EDTA salt comprising tetrasodium EDTA demonstrate both inhibitory and bactericidal activity against all of the microbial isolate populations tested. These results are highly unexpected in view of the literature, which doesn't suggest that tetrasodium EDTA, used as a stand-alone antimicrobial agent, has *bactericidal* (population killing) activity against *a broad spectrum of microorganisms*. It is urged that Applicants' pending claims involve an inventive step and are patentable over any combination of the prior art references relied upon for rejection in the Written Opinion. Reconsideration of the Examiner's Reasoned Statement is requested in advance of issuance of the International Preliminary Examination Report.

Respectfully submitted,

Ann W. Speckman
Registration No. 31,881

Date: July 1, 2004

SPECKMAN LAW GROUP PLLC

20601

What is claimed is:

1. A method for disinfecting a conduit by contacting the conduit with a disinfectant solution consisting essentially of an ethylene diamine tetraacetic acid (EDTA) salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have a bactericidal effect over a broad spectrum of microbes and a destructive effect against a variety of yeasts, and wherein the EDTA salt comprises tetrasodium EDTA.

2. The method of claim 1, wherein the solvent is water.

3. The method of claim 1, wherein the concentration of the EDTA salt is from about 5 to about 1,000 mg for each ml of solvent.

4. The method of claim 3, wherein the concentration of the EDTA salt is more than 10 mg for each ml of solvent.

5. The method of claim 1, wherein contacting the conduit with the disinfectant solution is accomplished by locking, flushing or coating the conduit with the disinfectant solution.

6. The method of claim 1, wherein the conduit is a conduit carrying sterile fluids, blood, plasma, or water.

7. The method of claim 1, wherein the conduit is in an airway support device.

8. The method of claim 1, wherein the conduit is a catheter.

9. The method of claim 1, wherein the conduit is a port.

10. The method of claim 9, wherein the port is a subcutaneous port.

11. The method of claim 1, wherein the conduit is a urological catheter.

12. A method for disinfecting an object by contacting the object with a disinfectant solution for an exposure period, the disinfectant solution consisting essentially of an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have a bactericidal effect over a broad spectrum of microbes and an inhibitory effect against a variety of yeasts, and wherein the EDTA salt comprises tetrasodium EDTA.

13. The method of claim 12, wherein the EDTA salt is at a concentration sufficient to have a destructive effect against a variety of yeasts.

14. The method of claim 12, wherein the object is selected from the group consisting of: medical instruments and devices, dental instruments and devices, veterinary instruments and devices, toothbrushes and contact lenses.

15. A method for disinfecting a catheter comprising:

introducing a disinfectant solution into an interior lumen of the catheter, wherein the disinfectant solution consists essentially of an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have bactericidal effect over a broad spectrum of microbes and inhibitory effect against a variety of yeasts, and wherein the EDTA salt comprises tetrasodium EDTA;

holding the disinfectant solution within the interior lumen for a selected period of time; and

removing the disinfectant solution from the interior lumen.

16. The method of claim 15, wherein the EDTA salt is at a concentration sufficient to have a destructive effect against a variety of yeasts.

17. The method of claim 15, wherein the concentration of the EDTA salt is from about 5 to about 1,000 mg for each ml of solvent.

18. The method of claim 15, wherein the concentration of the EDTA salt is more than 10 mg for each ml of solvent.

19. A disinfectant solution consisting essentially of an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have bactericidal effect over a broad spectrum of microbes and inhibitory effect against a variety of yeasts, and wherein the EDTA salt comprises tetrasodium EDTA .

20. The disinfectant solution of claim 19, wherein the EDTA salt is at a concentration sufficient to have a destructive effect against a variety of yeasts.

21. The disinfectant solution of claim 19, wherein the EDTA salt is in a concentration of at least 10 mg for each ml of solvent.

22. The disinfectant solution of claim 19, wherein the solvent is water.

23. A method for treating a biofilm by destroying the structure of the biofilm and killing or inhibiting the growth of individual organisms within the biofilm, by contacting the biofilm with a disinfectant solution consisting essentially of an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have a bactericidal effect over a broad spectrum of microbes, and wherein the EDTA salt comprises tetrasodium EDTA.

24. The method of claim 23, wherein the EDTA salt is at a concentration of at least 10 mg for each ml of solvent.

25. The method of claim 23, wherein the solvent is water.

EFFICACY OF DI- AND TETRA-SODIUM EDTA SOLUTIONS AGAINST VARIOUS CLINICAL ISOLATES

Organism ID	Di-sodium EDTA		Tetra-sodium EDTA	
	MIC	MBC	MIC	MBC
S24 Staph. epidermidis	<0.5	<0.5	<0.5	<0.5
31 Staph. epidermidis	<0.5	<0.5	<0.5	<0.5
301 Staph. xylosus	<0.5	<0.5	<0.5	20
300 Staph.capitis	<0.5	<0.5	<0.5	10
J46 Staph.lentus	<0.5	<0.5	<0.5	<0.5
S24 Staph.capitis	<0.5	<0.5	<0.5	<0.5
R8 Staph. simulans	<0.5	1	<0.5	1
72 S.aureus	<0.5	<0.5	<0.5	<0.5
R57 S.aureus	<0.5	10	<0.5	8
R13 S.aureus	<0.5	10	<0.5	<0.5
R30 S.aureus	<0.5	10	------	-------
8 S.aureus	<0.5	<0.5	------	------
R64 MRSA	<0.5	<0.5	<0.5	<0.5
R51 MRSA	<0.5	1	<0.5	<0.5
R92 MRSA	<0.5	10	<0.5	<0.5
S93 MRSA	<0.5	<0.5	<0.5	<0.5
J67 MRSA	<0.5	10	<0.5	<0.5
R8 VRE	<0.5	100	<0.5	30
Woods VRE	<0.5	100	<0.5	1
S77 Enterococcus Faecium	<0.5	100	<0.5	6

S76 Enterococcus faecalis	<0.5	100	<0.5	40
68 Klebsiella pneumoniae	8	60	6	6
R51 Klebsiella pneumoniae	------	------	-------	------
128 Klebsiella oxytoca	1	90	4	6
J7 Klebsiella ornitholytica	1	60	4	8
250 E. coli	1.5	80	1.5	1.5
B/C E. coli	------	------	-------	------
137 E. coli	4	60	2	2
292 Ent. cloacae	4	>100	6	15
190 Ent. cloacae	4	100	6	15
J22 Ent. cloacae	6	>100	6	10
R4 Steno. maltophilia	------	------	------	------
B/C Pseudomonas aeruginosa	------	------	------	------
J20 Pseudomonas aeruginosa	<0.5	50	2	4
J26 Pseudomonas sp.	<0.5	25	8	4
R75 Coryne. amycolatum	NG	NG	<0.5	20
R23 Coryne. strait/amy	NG	NG	<0.5	<0.5
177 Acinetobacter baumanii	<0.5	<0.5	<0.5	<0.5
J44 Acinetobacter baumanii	<0.5	1	<0.5	<0.5
R16 Proteus mirabilis	<0.5	50	<0.5	15
R81 Proteus vulgaris	<0.5	15	<0.5	8
R26 Proteus mirabilis	<0.5	50	1	15

CERTIFICATE OF EXPRESS MAILING
"Express Mail" Mailing Label No.: ED 043241468 US
I hereby certify that this paper or fee is being deposited with the United States Postal Service with sufficient postage as first class "Express Mail Post Office to Addressee" service under 37 C.F.R. 1.10 on the date indicated below and is addressed to MS: AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
Date of Deposit: August 31, 2004

Selena Whitaker-Paquiet

Attorney Docket No.: 13317.1001CIP
PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of **Peter KITE and David HATTON**

Group Art Unit: 1617

Application No. : 10/659,413

Filed : September 10, 2003

For : ANTISEPTIC COMPOSITIONS, SYSTEMS AND METHODS

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

MAIL STOP: AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir or Madam:

The attached form PTO/SB/08 (substitute for form 1449A/PTO) identifies 4 U.S. patent references and 1 literature reference. Copies of each of these references are enclosed herewith for the Examiner's convenience.

The documents listed on the accompanying form PTO/SB/08 are cited in compliance with the provisions of 37 C.F.R §§ 1.56, 1.97 and 1.98, as amended. Applicant does not concede that the references are "prior art" under 35 U.S.C. §102 or §103, and specifically reserves the right to antedate such materials, as by a showing under 37 C.F.R. § 1.131 or otherwise.

This Information Disclosure Statement is being filed prior to receipt of any substantive Office Action, and no fee or certification is therefore required.

Respectfully submitted,

Ann W. Speckman
Registration No. 31,881

Date: August 31, 2004

SPECKMAN LAW GROUP PLLC

20601

PTO/SB/08 (10-01)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 1

Complete if Known	
Application Number	10/659,413
Filing Date	September 10, 2003
First Named Inventor	Peter KITE and David HATTON
Art Unit	1617
Examiner Name	
Attorney Docket Number	13317.1001cip

U.S. PATENT DOCMENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] *(if known)*	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	1	US-6,762,160 B2	Jul. 13, 2004	Barbeau, et al.	
	2	US-6,423,706 B2	Jul. 23, 2002	Sodemann	
	3	5,910,420	Jun. 8, 1999	Tuompo, et al.	
	4	5,362,754	Nov. 8, 1994	Raad, et al.	
	5				
	6				
	7				
	8				
	9				
	10				

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country code[3] -Number [4]-Kind Code[5] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T[6]
	11					
	12					
	12					

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
	1	IZZAT, I.N., et al., "Effect of varying concentrations of EDTA on the antimicrobial properties of cutting fluid preservatives," *Microbios*, Vol. 26, No. 103, pp. 37-44 (1979)	
	2		
	3		
	4		
	5		

Examiner Signature		Date Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Applicant's unique citation designation number (optional). [2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

CERTIFICATE OF MAILING

I hereby certify that this paper or fee is being deposited with the United States Postal Service with sufficient postage as first class mail under 37 C.F.R. 1.8 on the date indicated below and is addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date: February 6, 2004

Selena Whitaker-Paquiet

Attorney Docket No.: 13317.1001cip

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re **Peter KITE** and **David HATTON**

Application No. : **10/659,413**

Filed : **September 10, 2003**

For : **ANTISEPTIC COMPOSITIONS, METHODS AND SYSTEMS**

INFORMATION DISCLOSURE STATEMENT

Commissioner For Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir or Madam:

The attached is a copy of a PTO/SB/08 (substitute for form 1449A/PTO) form that were filed in connection with a related patent application. The related patent application is U.S. Patent Application No. 10/313,844, filed December 5, 2002.

The documents listed on the accompanying PTO/SB/08 (substitute for form 1449A/PTO) form were cited in compliance with the provisions of 37 C.F.R §§ 1.56, 1.97 and 1.98, as amended. Applicants do not concede that the references are "prior art" under 35 U.S.C. §102 or 103, and specifically reserve the right to antedate such materials, as by a showing under 37 C.F.R. § 1.131 or otherwise. Copies of the cited references were filed in connection with the related application. Applicants will provide additional copies of these references if requested by the Examiner.

Applicants note that MPEP 2001.06(b) specifies that normally, if the application under examination is identified as a continuation-in-part of an earlier application, the Examiner will consider the art cited in the earlier application. Applicants respectfully request that the Examiner communicate to the Applicants that the art cited in the attached PTO-1449 and PTO-892 forms is made of record in the subject application.

Also attached is a form PTO/SB/08 (substitute for form 1449A/PTO) in connection with the subject application, which identifies 22 U.S. patent references, 3 U.S. patent application publication references, 5 international patent application publication references, 1 foreign patent reference and 9 literature references. Copies of each of these references are enclosed herewith for the Examiner's convenience.

The documents listed on the accompanying form PTO/SB/08 are cited in compliance with the provisions of 37 C.F.R §§ 1.56, 1.97 and 1.98, as amended. Applicant does not concede that the references are "prior art" under 35 U.S.C. §102 or §103, and specifically reserves the right to antedate such materials, as by a showing under 37 C.F.R. § 1.131 or otherwise.

This Information Disclosure Statement is being filed prior to receipt of any substantive Office Action, and no fee or certification is therefore required.

Respectfully submitted,

Ann W. Speckman
Registration No. 31,881

Date: February 6, 2004
SPECKMAN LAW GROUP
20601

PTO/SB/08 (10-01)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

				Complete if Known	
				Application Number	10/313,844
				Filing Date	December 5, 2002
				First Named Inventor	Peter KITE and David HATTON
				Art Unit	Unassigned
				Examiner Name	
Sheet	1	of	1	Attorney Docket Number	13317.1001

U.S. PATENT DOCMENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] *(if known)*	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	1	US-2003/0035779 A1	Feb. 20, 2003	Brown, et al.	
	2	US-2003/0032605 A1	Feb. 13, 2003	Raad, et al.	
	3	4,258,056	Mar. 24, 1981	Lentsch	
	4	5,008,202	Apr. 16, 1991	Edmondson, et al.	
	5	5,300,296	Apr. 5, 1994	Holly, et al.	
	6	5,688,516	Nov. 18, 1997	Raad, et al.	
	7	5,998,488	Dec. 7, 1999	Shinohara, et al.	
	8	6,077,501	Jun. 20, 2000	Sickora, et al.	
	9	US-6,174,537 B1	Jan. 16, 2001	Khan	
	10	US-6,423,348 B1	Jul. 23, 2002	Mickus	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country code[3] -Number [4]-Kind Code[5] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T[6]
	11	WO 00/72906 A1	Dec. 7, 2000	Becton, Dickinson and Company		
	12	WO 02/05188 A1	Jan. 17, 2002	Vasca, Inc.		
	12	WO 99/09997 A1	Mar. 4, 1999	Board of Regents U. of Texas		

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
	1	Root, Jennifer L. et al., "Inhibitory Effect of Disodium EDTA upon the Growth of *Staphylococcus epidermidis* In Vitro: Relation to Infection Prophylaxis of Hickman Catheters," *Antimicrobial Agents and Chemotherapy*, Vol. 32, No. 11, pp. 167-1631 (Nov. 1988)	
	2		
	3		
	4		
	5		

Examiner Signature		Date Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Applicant's unique citation designation number (optional). [2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

PTO/SB/08 (10-01)
oved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and T... ...mark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	1	of	3

Complete if Known	
Application Number	10/659,413
Filing Date	September 10, 2003
First Named Inventor	Peter KITE and David HATTON
Art Unit	
Examiner Name	
Attorney Docket Number	13317.1001cip

U.S. PATENT DOCMENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] *(if known)*	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	1	US-6,679,870 B1	20 Jan. 2004	Finch et al.	
	2	US-6,592,564 B2	15 Jul. 2003	Finch et al.	
	3	US-6,583,181 B1	24 Jun 20023	Chang et al.	
	4	US-6,569,852 B1	27 May 2003	Sodemann	
	5	US-6,509,319 B1	21 Jan. 2003	Raad et al.	
	6	US-6,498,157 B2	24 Dec. 2002	Sodemann	
	7	US-6,429,225 B1	6 Aug. 2002	Nagai et al.	
	8	US-6,350,251 B1	26 Feb. 2002	Prosl et al.	
	9	US-6,267,979 B1	31 Jul. 2001	Raad et al.	
	10	US-6,197,738 B1	6 Mar. 2001	Regutti	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country code[3] -Number [4]-Kind Code[5] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T[6]
	1	WO 02/072748 A1	19 Sep. 2002	S.C. Johnson & Son, Inc.		
	2	WO 02/062260 A2	15 Aug. 2002	Bio-Concept Laboratories		
	3	WO 00/30460	2 Jun. 2000	The Procter & Gamble Company		
	4	WO 00/27438	18 May 2000	University de Montreal		

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
	1	RAAD, Issam et al., "In Vitro and Ex Vivo Activities of Minocycline and EDTA Against Microorganisms Embedded in Biofilm on Catheter Surfaces," *Antimicrobial Agents and Chemotherapy*, Vol. 47, No. 11, pp. 3580-3585 (Nov. 2003)	
	2	KRANIAK, J.M. et al., "Effect of Ethylenediaminetetraacetic Acid (EDTA) and Metal Ions on Growth of *Staphylococcus aureus* 196E in Culture Media," *Journal of Food Science*, Vol. 53, No. 3, pp. 910-913 (1988)	
	3	GRAY, G.W. et al., "Effect of Ethylenediaminetetra-acetic Acid on the Cell Walls of Some Gram-Negative Bacteria," *J. Gen Microbiol.*, Vol. 39, pp. 385-399 (1965)	
	4	BHAGAT, Renu et al., "Growth Response of *Pseudomonas stutzeri* RS34 to Ethylenediaminetetraacetic (EDTA) and its Interaction with Zinc," *Indian Journal of Experimental Biology*, Vol. 31, pp. 590-594 (July 1993)	
	5	SAID, A.A. et al., "Expression of H1 Outer-Membrane Protein of *Pseudomonasaeruginosa* in Relation to Sensitivity to EDTA and Polymyxin B," *J. Med. Microbiol.*, Vol. 24, pp. 267-274 (1987)	

Examiner Signature		Date Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Applicant's unique citation designation number (optional). [2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	2	of	3

Complete if Known	
Application Number	10/659,413
Filing Date	September 10, 2003
First Named Inventor	Peter KITE and David HATTON
Art Unit	
Examiner Name	
Attorney Docket Number	13317.1001cip

U.S. PATENT DOCMENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] *(if known)*	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	11	US-6,187,768 B1	13 Feb. 2001	Welle et al.	
	12	US-6,166,007	26 Dec. 2000	Sodemann	
	13	US-6,165,484	26 Dec. 2000	Raad et al.	
	14	US-6,126,706	3 Oct. 2000	Matsumoto et al.	
	15	US-6,004,539	21 Dec. 1999	Longo, Jr. et al.	
	16	US-5,908,869	1 Jun, 1999	Jones et al.	
	17	US-5,820,607	13 Oct. 1998	Tcholakian et al.	
	18	US-5,731,356	24 Mar. 1998	Jones et al	
	19	US-5,180,749	19 Jan. 1993	Cusack et al.	
	20	US-4,847,004	11 Jul. 1989	McLeod	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country code[3] -Number [4]-Kind Code[5] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T[6]
	5	WO 96/39215	12 Dec. 1996	Board of Regents, Univ. of Texas System		
	6	EP 1 238 677 A2	11 Sep. 2002	AstraZeneca AB		
	7					
	8					

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
	6	HARPER, W.E.S. et al., "Effect of Chlorhexidine/EDTA/Tris Against Bacterial Isolates from Clinical Specimens," *Microbios*, Vol. 21, pp. 107-112 (1987)	
	7	HAQUE, H. et al., "Effect of Chelating Agents on the Susceptibility of Some Strains of Gram-Negative Bacteria to Some antibacterial Agents," *Antimicrobial Agents and Chemotherapy.*, Vol. 6, No. 2, pp. 200-206 (Aug. 1974)	
	8	HAQUE, H. et al., "Effect of Ethylenediaminetetraacetic Acid and Related Chelating Agents on whole Cells of Gram-Negative Bacteria," *Antimicrobial Agents and Chemotherapy.*, Vol. 5, No. 5, pp. 447-452 (May 1974)	
	9	RUSSELL, A.D., "Ethylenediaminetetra-acetic Acid," *National Library of Medicine, Bethesda, Maryland*, Academic Press Inc. (London) Ltd. pp. 209-224 (1971)	
	10		

Examiner Signature		Date Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Applicant's unique citation designation number (optional). [2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

PTO/SB/08 (10-01)
...ved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Tr... ...nark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	3	of	3

Complete if Known	
Application Number	10/659,413
Filing Date	September 10, 2003
First Named Inventor	Peter KITE and David HATTON
Art Unit	
Examiner Name	
Attorney Docket Number	13317.1001cip

U.S. PATENT DOCMENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] *(if known)*	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	21	US-4,258,056	24 Mar. 1981	Lentsch	
	22	US-2,474,412	28 Jun. 1949	Bersworth	
	23	US-2002/0111346 A1	15 Aug. 2002	Sodemann	
	24	US-202/0010438 A1	24 Jan. 2002	Finch et al.	
	25	US-2001/0003746 A1	14 Jun. 2001	Sodemann	
	26				
	27				
	28				
	29				
	30				

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country code[3] -Number [4]-Kind Code[5] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T[6]

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
	1		
	2		
	3		
	4		
	5		

Examiner Signature		Date Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Applicant's unique citation designation number (optional). [2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231 DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

PATENTS AND LITERATURE CITED IN PETITION TO MAKE SPECIAL

In re application of **Peter KITE and David HATTON**
Application No. : 10/659,413
Filed : September 10, 2003
For : **ANTISEPTIC COMPOSITIONS, SYSTEMS AND METHODS**
Our Ref. No. : 13314.1001cip

COUNTRY	PATENT / PUBLICATION NUMBER
US	2,474,412
US	4,258,056
US	4,847,004
US	5,008,202
US	5,300,296
US	5,362,754
US	5,688,516
US	5,908,869
US	5,910,420
US	5,998,488
US	6,004,539
US	6,077,501
US	6,165,484
US	6,166,007
US	6,187,768
US	6,197,738
US	6,267,979
US	6,350,251
US	6,423,348
US	6,423,706
US	6,429,225
US	6,498,157
US	6,509,319
US	6,569,852
US	6,583,181
US	6,592,564
US	6,679,870
US	6,762,160
US	2003/0032605
WO	99/09997
WO	00/27438
WO	00/30460
WO	00/72906 A1
WO	02/05188
WO	02/062260

WO	02/072748

LITERATURE CITATIONS
BHAGAT, R. et al., "Growth Response of *Pseudomonas stutzeri* RS34 to Ethylenediaminetetraacetic (EDTA) and its Interaction with Zinc," *Indian Journal of Experimental Biology*, Vol. 31, pp. 590-594 (July 1993)
GRAY, G.W. et al., "The Effect of Ethylenediaminetetra-acetic Acid on the Cell Walls of Some Gram-Negative Bacteria," *Journal of Genetic Microbiology,* Vol. 39, pp. 385-399 (1965)
HARPER, W.E.S., et al., "Effect of chlorhexidine/EDTA/Tris Against Bacterial Isolates from Clinical Specimens," *Microbios*, Vol. 21, pp. 107-112 (1987)
HAQUE, H. et al., "Effect of Chelating Agents on the Susceptibility of Some Strains of Gram-Negative Bacteria to Some Antibacterial Agents," *Antimicrobial Agents and Chemotherapy,* Vol. 67, No. 2, pp. 200-206 (Aug. 1974)
HAQUE, H. et al., "Effect of Ethylenediaminetetra-acetic Acid and Related Chelating Agents on Whole Cells of Gram-Negative Bacteria," *Antimicrobial Agents and Chemotherapy,* Vol. 5, No. 5, pp. 447-452 (May 1974)
IZZAT and BENNETT, "Effect of varying concentrations of EDTA on the antimicrobial properties of cutting fluid preservatives," Microbios 26:37-44 (1979)
KRANIAK, J.M.., et al. "Effect of Ethylenediaminetetraacetic Acid (EDTA) and Metal Ions on Growth of *Staphylococcus aureus* 196E in Culture Media," *Journal of Food Science*, 1988, pp. 910-913 (1988)
ROOT, J. et al., "Inhibitory Effect of Disodium EDTA upon the Growth of *Staphylococcus epidermidis* In Vitro: Relation to Infection Prophylaxis of Hickman Catheters," *Antimicrobial Agents and Chemotherapy*, Vol. 32, No. 11, pp. 1627-1631 (Nov. 1988)
RUSSELL, A.D., "*Ethylenediaminetetra-acetic Acid*," National Library of Medicine, Bethesda, Maryland, Academic Press Inc. (London) Ltd. pp. 209-224 (1971)